REMARKS

Claims 80-84, 87-95, 97-98 and 103-112 are pending in the instant application. Claims 80-84, 87-95, 97-98 and 103-112 have been rejected. Reconsideration is respectfully requested in light of the following remarks and Dr. Simpson's Declaration submitted herewith.

I. Rejection of Claims 80-84, 87-95, 97-98 and 103-112 under 35 U.S.C. 112, first paragraph

The rejection of claims 80-84, 87-95 and 97-98 under 35 U.S.C. 112, first paragraph, for lack of enablement has been maintained in part and applied to claims 103-112. The Examiner has acknowledged the specification to be enabling for a method of assessing skeletal muscle damage in a subject comprising detecting hypoxemia-induced skeletal troponin I (sTnI) peptide fragment with a molecular mass of 17 kDa and/or a 42 kDa covalent complex comprising sTnI with MAb C5 or a hypoxemia-induced skeletal troponin T (sTnT) peptide fragment with a molecular mass of 28 kDa with MAb JLT-12 (and antibodies disclosed in the prior art as capable of binding sTnI and sTnT) in skeletal muscle (including the diaphragm) or alternatively assessing skeletal muscle damage in a subject comprising detecting hypoxemia-induced modified sTnI having a molecular mass of 66 kDa or 26 kDa in urine.

However, the Examiner suggests that the specification does not reasonably provide enablement for the claims as broadly recited.

Amendments by Applicants in the response filed July 27, 2007 have been acknowledged by the Examiner to overcome issues relating to antibody fragments and the biological sample. However, the Examiner suggests that the Declaration under 37 C.F.R. 1.132 filed July 27, 2007 was insufficient to overcome the remaining issues.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants are submitting herewith a second Declaration by Dr. Jeremy Simpson addressing the insufficiencies in the prior Declaration outlined by the Examiner in the instant Office Action.

Specifically, as discussed in paragraph 3 of Dr. Simpson's Declaration, the data presented originally in Figures 1A and 1B of the July 27, 2007 Declaration have been separately presented in Figures 1 and 2. Data presented originally in Figure 2 of the July 27, 2007 Declaration is now presented in Figure 3. These changes to the Figure numbering were made to better clarify experiments presented in each Figure and to address questions raised by the Examiner. No new data is presented in the Declaration submitted herewith.

As made clear in paragraph 4 of Dr. Simpson's Declaration submitted herewith, data presented in Figures 1 through 3 were generated from serial serum samples obtained from multiple patients with various muscle injuries, i.e. trauma seizures and drug-induced rhabdomyolysis.

As discussed in detail in paragraph 5 of Dr. Simpson's Declaration submitted herewith, Figure 1 shows representative Western blots of serial serum samples from 5 different patients probed for fsTnI. Each of the 5 patients had been admitted to the hospital with indications of skeletal muscle disorders. For clarity, the blots have been labeled Patient 1 through Patient 5. Also now labeled on each blot as time 0 is the first blood sample taken upon hospital admission (see left-hand lane of each blot) and the region of the blots with degradation products. Clear now from Figure 1 and paragraph 5 of Dr. Simpson's Declaration submitted herewith is:

(1) the data for "time 0";

(2) the blots as now labeled show clear correspondence for each patient and that there is no control; and

(3) that Patients 1 and 2 had detectable levels of fsTnI degradation products detected using fsTnI specific mAb F1-32, a commercially available antibody as of the filing date of the instant application.

Further, as discussed in paragraph 6 of Dr. Simpson's Declaration provided herewith, Figure 2, showing representative Western blots from 6 additional patients, has been modified to include labels for each patient and arrows adjacent to blots of Patients 6, 9 and 11 highlighting at least 7 different proteolytic fragments of fsTnI. As stated in paragraph 6 of Dr. Simpson's Declaration, these proteolytic fragments of fsTnI were also detected using anti fsTnI specific mAb F1-32. Shown beneath each blot in Figure 2 are creatinine kinase levels measured for each of Patients 6 through 11 (see paragraph 6 of Dr. Simpson's Declaration submitted herewith). Made clear by these levels is that there is no correlation between creatinine kinase levels in a patient and the presence and number of proteolytic fragments of fsTnI in that patient. Clear now from Figure 2 and paragraph 6 of Dr. Simpson's Declaration submitted herewith is:

(1) what each sample in Figure 2 corresponds to; and

(2) what each lane represents and that there is no control, but rather data for 6 additional patients.

Paragraph 7 of Dr. Simpson's Declaration addresses questions raised by the Examiner concerning data presented in original Figure 2, now re-labeled as Figure 3. As stated in paragraph 7 of Dr. Simpson's Declaration submitted

herewith, Figure 3 shows two Western blots of serial serum samples obtained over a three day period from a single patient suffering from skeletal muscle damage resulting from seizures. Each lane of the gels represents a different serum sample obtained from the same patient in time sequential order over the 3 day period [2 samples on day 1, 4 samples on day 2, 2 samples on day 3]. In the top blot of Figure 3, the samples were probed with anti-fsTnI specific mAb F1-32, commercially available as of the filing date of this patent application from Spectral Diagnostics. In the bottom blot of Figure 3, the same samples were probed with anti-fsTnI specific mAb SI-1, commercially available as of the filing date of this patent application from Hytest. At least one proteolytic fragment with a molecular weight between 20 and 26.6 kDa was detectable in the serum of the patient over time with both antibodies (see Figure 3 and paragraph 7 of Dr. Simpson's Declaration submitted herewith). Accordingly, paragraph 7 of Dr. Simpson's Declaration clarifies:

(1) what the different lanes of each gel represent; and

(2) the antibodies, used, their specificity for fsTnI, and their commercial availability as of the filing date of the instant application.

Thus, as summarized in paragraph 8 of Dr. Simpson's Declaration submitted herewith, Figures 1-3, as re-presented for clarification purposes, show detection of multiple proteolytic fragments of fsTnI in the molecular weight range of 20 to 26.6 kDa in serum of human patients suffering from various skeletal muscle disorders. Accordingly, limitation of the claims to the two exemplary fragments disclosed in the specification should not be required.

Further, Dr. Simpson's Declaration submitted herewith makes clear that two additional anti-fsTnI specific mAbs to that exemplified in the instant application, both of which were commercially available as of the filing date of the instant application, can be used to detect multiple proteolytic fragments of fsTnI. Accordingly, limitation of the claims to specific exemplary antibodies disclosed in the specification should not be required.

Finally, as clearly demonstrated by Dr. Simpson's Declaration submitted herewith, and the experiments described therein conducted similarly to the procedures set forth at pages 28-30 of the instant patent application (see paragraph 8 of Dr. Simpson's Declaration submitted herewith), contrary to the Examiner's suggestion, undue experimentation was not required to practice to make and use the invention in its full scope.

Withdrawal of this rejection under 35 U.S.C. 112, first paragraph, is respectfully requested.

II. Provisional Obviousness-type Double Patenting Rejection

The rejection of claims 80-84 and 92-98 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 16-18, 20-28, 31, 34-35 and 37-41 of copending Application No. 09/419,901 has been maintained. Further, this rejection has been applied to new claims 103-112. Applicants respectfully disagree that claims of the instant application drawn to methods for detecting a **peptide fragment** of a myofilament protein; or a covalent or non-covalent complex of at least a **peptide fragment** of a myofilament protein and an intact myofilament protein; or two **peptide fragments** of myofilament proteins are obvious over claims drawn to detecting a myofilament protein modification product wherein at least one myofilament protein modification product is a **chemical adduct** of a myofilament protein. However, in an earnest effort to advance the prosecution of this case, Applicants are submitting herewith a terminal disclaimer with respect to copending Application No. 09/419,901.

Accordingly, withdrawal of this provisional obviousness-type double patenting rejection is respectfully requested.

The provisional obviousness-type double patenting rejection over claims 38, 39, 40, 41, 42, 43, 44, 45 and 46 of copending Application No. 11/138,184, has also been maintained.

Applicants respectfully traverse this rejection.

As already pointed out in the response filed July 27, 2007, the filing date of Application No. 11/138,184 is later than the instant application. Accordingly, as the term of the patent runs from the filing date of the application, it is Application No. 11/138,184 which may require a terminal disclaimer with respect to the instant application should there be overlapping claims. To date, Applicants have not received an Office Action in Application No. 11/138,184 on the merits of patentability. However, the pending application is of record via citation in an Information Disclosure Statement submitted in Application No. 11/138,184. Thus, should the Examiner in Application No. 11/138,184 determine that there is an overlap in the claimed subject matter during prosecution of that application, Applicants can file a Terminal Disclaimer in Application No. 11/138,184 to address this issue.

Further, claims 38, 39, 40, 41, 42, 43, 44, 45 and 46 of copending Application No. 11/138,184 are drawn to methods of diagnosing, monitoring, or differentially diagnosing skeletal muscle damage in a subject, comprising characterizing two or more **isoforms** of a myofilament protein, or a modification product thereof, not to detecting a skeletal troponin I **peptide fragment**, or a skeletal troponin T **peptide fragment** as claimed in the instant application. Accordingly, Applicants respectfully disagree that the pending claims are obvious over claims 38, 39, 40, 41, 42, 43, 44, 45 and 46 of copending Application No. 11/138,184.

Withdrawal of this provisional obviousness-type double patenting rejection over Application No. 11/138,184 is therefore also respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

Kathleen A. Tyrrell
Registration No. 38,350

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Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515